

How to optimize the global stem cell donor pool: analyses based on unsuccessful donor searches

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Overview

Despite around 40 million registered stem cell donors worldwide, it is not always possible to find a full HLA match for a patient in need of HSCT. Between May 2019 and May 2021, 22 partner registries sent high-resolution search requests for 5,907 patients via EMDIS to the DKMS Registry and agreed to the scientific analysis and publication of these data in anonymized form. Until May 2021, no 10/10 matched donor was identifiable for 2,205 of these patient cases in the DKMS donor pool (without DKMS US) of about 10 million donors (see Figure 1).

Methods

To investigate how donors might be found for patients with these particular genotypes via additional donor recruitment, we estimated 5-locus HLA haplotype frequencies for 67 populations from 62 countries based on DKMS donors' self-assigned ethnic background. US donors were grouped into four populations (African-American, Asian/Pacific-Islanders, Caucasian, Hispanic). For donors from South Africa, three populations have been used (Black, Coloured, White).

Sample sizes were restricted to 1,000 donors in order to avoid bias from sample size differences. We used Hapl-o-Mat, our freely-available, open-source implementation of the EM algorithm (<https://github.com/DKMS/Hapl-o-Mat>), for haplotype frequency estimation.

Haplotypes with estimated frequencies smaller than $\frac{1}{271} = 0.0005$ (corresponding to a count of less than 1 in the sample) were not considered in the further analyses.

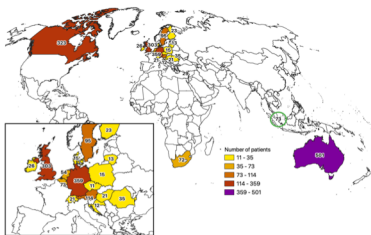


Figure 1 Origin and number of patient search requests without a 10/10 match.

In a first scenario, we constructed any possible genotype from the entire set of haplotypes and checked which patient genotypes could be obtained.

In a second scenario, we required that both haplotypes to form a matching genotype originated from the same population.

As a third scenario, we estimated for how many patients a suitable donor could be found if a given number of donors were to be recruited.

Results

In the first scenario, a matching genotype could be constructed for 1,446 of the 2,205 for the patients (65.6%).

In the second scenario, we have been able to find a matching genotype for 807 patients (36.6%). The populations from whose haplotypes the most patient-matching genotypes could be constructed were Chinese (68), Thai (66), Asian/Pacific-Islanders (US) (54) and Vietnamese (52).

For the third scenario, we investigated cases where 100,000, 200,000, or 500,000 individuals could be recruited in each of the individual populations. Table 1 presents the number of patients that could find a match among the newly recruited donors.

Population	Number of recruited donors			Population	Number of recruited donors		
	100,000	200,000	500,000		100,000	200,000	500,000
Austria	5	7	13	Iran	6	8	12
USA African	5	6	9	Ireland	5	10	14
Alghbanistan	5	8	11	Iraq	2	3	5
Albania	7	8	14	Kosovo	6	8	11
USA Asian	25	31	36	Kirgistan	7	10	15
Armenia	4	7	10	Luxembourg	3	5	9
Belgium	5	10	15	Lithuania	6	8	13
Bulgaria	6	9	14	Morocco	6	10	15
Bosnia	9	11	17	Mexico	1	2	6
ZA Black	7	8	10	North Macedonia	6	8	13
Brazil	5	8	14	Netherlands	3	5	9
Belarus	3	5	8	Portugal	5	6	12
Switzerland	8	12	20	Peru	2	4	6
Sri Lanka	2	3	5	Pakistan	7	11	16
Colombia	4	5	8	Poland	4	7	15
ZA Coloured	7	9	13	Chile	3	5	6
Czech Rep.	5	8	12	Libanon	4	7	11
Germany	3	6	10	Romania	6	10	16
Denmark	4	7	12	South Korea	13	16	19
Algeria	5	9	15	Philippines	19	22	29
Spain	4	7	15	Sweden	8	11	19
Eritrea	2	3	5	Slovakia	3	5	7
Egypt	3	5	7	Slovenia	5	7	11
USA Caucas.	3	6	9	Serbia	6	10	16
France	5	9	14	Spain	4	8	13
Finland	7	9	14	Thailand	28	36	43
United Kingdom	4,1	6,6	11,4	Tunisia	2	5	8
Ghana	4,3	6	9,1	Turkey	6	9	17
Greece	4,6	9	15,3	Ukraine	6	9	13
Hungary	6,7	10,5	16	Vietnam	29	33	37
USA Hispanic	3,2	5,4	8,1	China	30	36	46
Croatia	5,1	8,5	11,8	Nigeria	4	7	9
Italy	5,1	8,7	12	ZA White	7	11	15
India	6,2	9,5	10,5				

Table 1 Number of patients with a match if a given number of donors is recruited in the respective population.

Outlook

To understand even better how the global stem cell donor pool can be improved, we plan to investigate how many patients would find a match if a number of new donors were to be recruited optimally among potential populations.

